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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| HILL, KEVIN KAI | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1633 | |

DATE MAILED: 04/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/524,827 | SAUER ET AL. | |
| | Examiner | Art Unit | |
| | Kevin K. Hill, Ph.D. | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-46* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Restriction is required under 35 U.S.C. 121 and 372.
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.
In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Invention I, claims 1-38, drawn to a process for preparing ketocarotenoids by cultivating genetically modified organisms having modified ketolase activity, and a genetically modified organism having modified ketolase activity caused by a ketolase comprising the amino acid sequence SEQ ID NO:2.

Invention II(a), claims 39-42, drawn to a ketolase comprising the amino acid sequence SEQ ID NO:8, with the proviso that the amino acid SEQ ID NO:4 is not present.

Invention II(b), claims 40, drawn to a ketolase comprising the amino acid sequence SEQ ID NO:6.

Invention II(c), claims 41, drawn to a ketolase comprising the amino acid sequence SEQ ID NO:12, with the proviso that the amino acid sequence SEQ ID NO: 6 is not present.

Invention II(d), claims 42, drawn to a ketolase comprising the amino acid sequence SEQ ID NO:49, with the proviso that the amino acid sequence SEQ ID NO: 47 is not present.

Invention III, claim 43, drawn to a nucleic acid encoding a protein of SEQ ID NO:8, with the proviso that the amino acid sequence SEQ ID NO:4 is not present; and furthermore, with the proviso that the sequence SEQ ID NO:5 is not present.

Invention IV(a), claims 44, drawn to a protein comprising the amino acid sequence of SEQ. ID NO: 4.

Invention IV(b), claims 45, drawn to a protein comprising the amino acid sequence of SEQ. ID NO: 6.

Invention IV(c), claims 46, drawn to a protein comprising the amino acid sequence of SEQ. ID NO: 47.

2. The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical feature for the following reasons:

37 CFR 1.475(c) states:

"If an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b) of this section, unity of invention might not be present."

37 CFR 1.47(d) also states:
"If multiple products, processes of manufacture, or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each of the other categories related thereto will be considered as the main invention in the claims, see PCT article 17(3)(a) and 1.476(c)."

In the instant application, Groups II, III and IV constitute additional products of Group I. Accordingly, restriction of Groups I-IV is proper.

A 371 case is considered to have unity of invention only when there is a technical relationship among those inventions involving one or more of the same or corresponding technical features. The expression "special technical feature' means those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. In the instant application, the linking technical feature of an organism genetically modified with a nucleotide functionally encoding a ketolase comprising the amino acid sequence of SEQ ID NO:2 does not constitute a contribution over the prior art.

Groups I-IV are drawn to multiple distinct products. The claimed inventions of Group I comprise genetically modified organisms having modified ketolase activity caused by a ketolase having the amino acid sequence of SEQ ID NO:2. The claimed inventions of Groups II(a)-(d) consist of ketolases defined by structurally distinct amino acid sequences. The claimed inventions of Groups IV(a)-(c) consist of proteins that have undisclosed properties of ketolases. The Group III invention is a structurally distinct nucleic acid. Applicants are reminded that nucleic acid sequences encoding different proteins, and the amino acid sequences they encode, are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleic acid and amino acid sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq. Therefore, there is no special technical feature linking the recited groups, as would be necessary to fulfill the requirement for unity of invention.

3. **Should Applicant elect Invention I**, a group restriction is required under 35 U.S.C. 121 and 372. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Invention I detailed above reads on patentably distinct inventive groups drawn to multiple enzymes comprising the amino acid sequences SEQ. ID NO:2, SEQ. ID NO:16, SEQ. ID NO:18,

respectively, and derivatives thereof. According to PCT Rule 13.2 and to the guidelines in Section (f)(i)(A) of Annex B of the PCT Administrative Instructions, all alternatives of a Markush Group must have a common property or activity. Although the ketolases recited in Claims 1, 3-4, 6-7, and 25-29 have a common structure in that they comprise the amino acid sequence of SEQ. ID NO:2, the ketolases are not regarded as being of similar nature because all of the alternatives do not share a common property or activity. Similarly, the hydroxylases recited in Claims 9-12 and 30 have a common structure in that they comprise the amino acid sequence of SEQ. ID NO:16, but the hydroxylases are not regarded as being of similar nature because all of the alternatives do not share a common property or activity. And, the β-cyclases recited in Claims 9-10, 14 and 30 have a common structure in that they comprise the amino acid sequence of SEQ. ID NO:18, but the β-cyclases are not regarded as being of similar nature because all of the alternatives do not share a common property or activity.

Applicants recite structural alterations to the respective reference SEQ. ID technical features, including undisclosed substitutions, deletions and insertions of amino acids. An amino acid sequence with at least 42% identity to SEQ ID NO:2 comprises amino acid sequences that are up to 58% non-identical to the SEQ. ID NO:2 technical feature. An amino acid sequence with at least 20% identity to SEQ ID NO:16 or SEQ ID NO:18, respectively, comprises amino acid sequences that are up to 80% non-identical to the SEQ. ID NO:16 or SEQ ID NO:18 technical features, respectively. Applicants are reminded that nucleic acid sequences encoding different proteins, and the amino acid sequences they encode, are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleic acid and amino acid sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq. Furthermore, Applicant does not require the adulterated polypeptide molecules derived from the parent SEQ. ID NO. to retain the biological functionality of the parent enzyme.

A search for SEQ. ID NO:2 would not be co-extensive with a search for an amino acid sequence containing unspecified structural differences, yet retaining at least 42% identity to SEQ. ID NO:2. Further, a reference rendering SEQ. ID NO:16 as anticipated or obvious over the prior art would not necessarily also render an amino acid sequence containing unspecified structural differences, yet retaining at least 42% identity to SEQ. ID NO:16 as anticipated or obvious over the prior art. Similarly, a finding that SEQ. ID NO:18 was novel and unobvious over the prior art would not necessarily extend to a finding that an amino acid sequence containing unspecified structural differences, yet retaining at least 42% identity to SEQ. ID NO:18 was also novel and unobvious over the prior art.

In response to the restriction requirement, Applicant must further elect a single ketolase (See Claim 1, for example), specifically:

a) a ketolase comprising the amino acid sequence SEQ. ID NO:2, or

a') an amino acid sequence derived from SEQ. ID NO:2, which has an identity of at least 42% at the amino acid level with the sequence SEQ. ID NO:2.

In response to the restriction requirement, Applicant must further elect a single hydroxylase (See Claim 12, for example), specifically:

b) a hydroxylase comprising the amino acid sequence SEQ. ID NO:16, or

b') an amino acid sequence derived from SEQ. ID NO:16, which has an identity of at least 20% at the amino acid level with the sequence SEQ. ID NO:16.

In response to the restriction requirement, Applicant must further elect a single β-cyclase (See Claim 14, for example), specifically:

c) a β-cyclase comprising the amino acid sequence SEQ. ID NO:18, or

c') an amino acid sequence derived from SEQ. ID NO:18, which has an identity of at least 20% at the amino acid level with the sequence SEQ. ID NO:18.

**Should Applicant elect Invention I**, a further group restriction is required under 35 U.S.C. 121 and 372. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Invention I detailed above reads on patentably distinct inventive groups drawn to multiple organisms. According to PCT Rule 13.2 and to the guidelines in Section (f)(i)(A) of Annex B of the PCT Administrative Instructions, all alternatives of a Markush Group must have a common property or activity. Although the organisms recited in Claims 18-23 and 32-36 have a common structure in that they are cellular, the organisms are not regarded as being of similar nature because all of the alternatives do not share a common property or activity. The modified organisms of Claims 18-23 and 32-36 do not share a common core structure or function, thus the species are patentably distinct. One of ordinary skill in the art could readily consult any cell biology reference textbook (e.g., Molecular Biology of the Cell, Alberts et al., Garland Publishing) describing the structure, characteristics and biological properties for each of the organisms, and would appreciate that based on such reference disclosures alone or in combination, that these organisms are distinct and separate.

A search for yeast would not be co-extensive with a search for plants. Further, a reference rendering Amaryllidaceae as anticipated or obvious over the prior art would not necessarily also render Malvaceae as anticipated or obvious over the prior art. Similarly, a finding that Marigold was novel and unobvious over the prior art would not necessarily extend to a finding that Zinnia was also novel and unobvious over the prior art.

In response to the restriction requirement, Applicant must further elect a single organism selected from the group consisting of bacteria, yeasts, algae fungi or plants (see Claims 18-19, for example).

**Should Applicant elect Invention I** and a microorganism, a further group restriction is required under 35 U.S.C. 121 and 372. In response to the restriction requirement, Applicant must further elect a single microorganism selected from the group consisting of microorganisms (1)-(24), as recited in Claims 20 and 34.

**Should Applicant elect Invention I** and a plant, a further group restriction is required under 35 U.S.C. 121 and 372. In response to the restriction requirement, Applicant must further elect a single plant family selected from the group consisting of plant families (1)-(28), as recited in Claims 22 and 35.

**Should Applicant elect Invention I** and a plant family from above, a further group restriction is required under 35 U.S.C. 121 and 372. In response to the restriction requirement, Applicant must further elect a single plant genera selected from the group consisting of plant genera (1)-(91), as recited in Claims 23 and 36.

It is further noted that these are group restriction requirements and should not be construed as election of species.

4. **Should Applicant elect Invention I** and an organism from above, a species restriction is further required under 35 U.S.C. 121 and 372.

This application contains claims directed to more than one species of genetically modified organisms as recited in Claims 2, 5, 16-17, 25-27 and 30-31 of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

a) wherein the organism, as wildtype, already has ketolase activity, or

b) wherein the organism, as wildtype, has no ketolase activity.

The claims are deemed to correspond to the species listed above in the following manner:

Claim 1, and claims dependent therefrom correspond to all the species listed above.

The following claim(s) are generic: 2, 5, 16-17, 25-27 and 30-31.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

As the technical feature (an organism) linking the members do not constitute a special technical feature as defined by PCT Rule 13.2, particularly since each of the species does not share a substantially common structural feature or function, the requirement for unity of invention is not fulfilled.

The species are drawn to multiple organisms that are structurally, genetically and physiologically distinct.

Applicant is required to elect a single named species as listed in the cited claims to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

**Should Applicant elect Invention I** and an organism from above, a species restriction is further required under 35 U.S.C. 121 and 372.

This application contains claims directed to more than one species of genetically modified organisms as recited in Claims 1-15, 17, and 25-31 of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species of genetically modified organisms are as follows:

i) genetically modified with ketolase (a), comprising the amino acid sequence SEQ. ID NO:2 from above,

ii) genetically modified with ketolase (a), comprising the amino acid sequence SEQ. ID NO:2 and hydroxylase (b), comprising the amino acid sequence SEQ. ID NO:16 from above,

iii) genetically modified with ketolase (a), comprising the amino acid sequence SEQ. ID NO:2 and β–cyclase (c), comprising the amino acid sequence SEQ. ID NO:18 from above,

iv) genetically modified with ketolase (a), comprising the amino acid sequence SEQ. ID NO:2 and hydroxylase (b') derived from SEQ. ID NO:16, which has an identity of at least 20% at the amino acid level with the sequence SEQ. ID NO:16, from above,

v) genetically modified with ketolase (a), comprising the amino acid sequence SEQ. ID NO:2 and β–cyclase (c') derived from SEQ. ID NO:18, which has an identity of at least 20% at the amino acid level with the sequence SEQ. ID NO:18 from above,

vi) genetically modified with ketolase (a') derived from SEQ. ID NO:2, which has an identity of at least 42% at the amino acid level with the sequence SEQ. ID NO:2 from above,

vii) genetically modified with ketolase (a') derived from SEQ. ID NO:2, which has an identity of at least 42% at the amino acid level with the sequence SEQ. ID NO:2 and hydroxylase (b), comprising the amino acid sequence SEQ. ID NO:16 from above,

viii) genetically modified with ketolase (a') derived from SEQ. ID NO:2, which has an identity of at least 42% at the amino acid level with the sequence SEQ. ID NO:2 and β–cyclase (c), comprising the amino acid sequence SEQ. ID NO:18 from above,

ix) genetically modified with ketolase (a') derived from SEQ. ID NO:2, which has an identity of at least 42% at the amino acid level with the sequence SEQ. ID NO:2 and hydroxylase (b') derived from SEQ. ID NO:16, which has an identity of at least 20% at the amino acid level with the sequence SEQ. ID NO:16 from above, or

x) genetically modified with ketolase (a') derived from SEQ. ID NO:2, which has an identity of at least 42% at the amino acid level with the sequence SEQ. ID NO:2 and β–cyclase (c') derived from SEQ. ID NO:18, which has an identity of at least 20% at the amino acid level with the sequence SEQ. ID NO:18 from above.

The claims are deemed to correspond to the species listed above in the following manner:

Claim 1, and claims dependent therefrom correspond to all the species listed above.

The following claim(s) are generic: 1-15, 17, and 25-31.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

As the technical feature (a polypeptide comprising the amino acid sequence of SEQ ID NO:2) linking the members does not constitute a special technical feature as defined by PCT Rule 13.2, particularly since each of the species does not share a substantially common structural feature or function, the requirement for unity of invention is not fulfilled.

The species are drawn to multiple organisms that are structurally, genetically and physiologically distinct. The genetically modified organisms [ii, iv, vii and ix] are metabolically enhanced by a distinctly different biochemical means than the organisms [iii, v, viii and x] and organisms [i and vi], and thus each organism species [i-x] is structurally different. Applicant is required to elect a single named species as listed in the cited claims to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their divergent subject matter, restriction for examination purposes as indicated is proper.

Thus, it would be unduly burdensome for the examiner to search all the claimed inventions being sought in the pending claims.

Applicant is advised that the reply for this requirement to be complete must include an election of the invention to be examined even though the requirement may be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin K. Hill, Ph.D. whose telephone number is 571-272-8036.

The examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DAVE TRONG NGUYEN
SUPERVISORY PATENT EXAMINER